

Ex. 5

Report of Shmuel Shoham, M.D. Regarding Box Hill Surgery Center Clinic Patient Fungal Infection Outbreak

I have been asked to provide expert opinion on behalf of Brenda Lee Rozek, a patient treated at Box Hill Surgery Center by Ritu Bhambhani, M.D. in 2012. This report supplements my September 15, 2016 report regarding Dr. Bhambhani's patients and reflects my expert opinion, to a reasonable degree of medical probability that the injection with the contaminated PF-MPA administered to her, led to Brenda Lee Rozek's fungal infection and to her death.

In my September 2016 report I also expressed my opinion as a licensed physician in Maryland that the method and manner in which PF-MPA from NECC was prescribed, ordered and administered at Box Hill Surgery Center by Dr. Bhambhani failed to conform to the standards of care for doctors in Maryland on prescribing and administering prescription medications to patients. Since then, I have read her additional deposition testimony regarding administration of MPA Brenda Rozek. This additional information confirms the opinions expressed in my earlier report.

Professional Qualifications:

I am an Associate Professor of Medicine at Johns Hopkins University School of Medicine and Associate Director of the Transplant and Oncology Infectious Diseases program at that institution. I am certified by the American Board of Internal Medicine in Infectious Diseases, and am licensed to practice medicine in the State of Maryland and the District of Columbia. I have over 17 years of experience in management of patients with invasive fungal infections, and am the author or co-author of over 100 original articles, book chapters and topic reviews, including publications directly related to the fungal infection outbreak associated with the contaminated PF-MPA injections. I serve as a reviewer and expert consultant to multiple journals, professional societies and government agencies in the US and abroad and am a member of professional guideline committees for the American Society of Transplantation (AST), the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and Infectious Diseases Mycoses Study Group (EORTC/MSG) and the National Comprehensive Cancer Network (NCCN). In 2015 the Washington, DC Chapter of the American College of Physicians honored my commitment to excellence in medical care and service to the College with their highest award, the John F. Maher Memorial Laureate Award. In 2017, I completed specialized training in reducing patient harm and graduated from the Armstrong Institute Patient Safety and Quality Improvement Leadership Academy, Johns Hopkins Medicine. My *Curriculum Vitae*, is attached and includes a list of publications I have authored.

Prior Expert Testimony:

In the past 4 years I have testified as an expert as follows:

- By deposition on August 11, 2016 and at trial in United States District Court, District of Massachusetts (on October 13, 2016) in the case of Barbara J. Bradley vs. David J. Sugarbaker.
- By deposition on January 19, 2017 in *In Re: New England Compounding Pharmacy, Inc. Products Liability Litigation, MDL No. 2419*, United States District Court For the Eastern District of Massachusetts.
- By deposition on August 2, 2017 in Case No. 15-C-464-3; Robert L. Snider vs. Wright Medical Technology Inc. and Dino J. Delaportas, M.D., AND Wright Medical Technology, Inc. as Third-Party Plaintiffs vs. United Hospital Center, INC. as Third-Party Defendants.
- By deposition on December 14, 2017 in The Matter Of: *Robinson v. Regional Hematology and Oncology, P.A.*

The specific case of Brenda Rozek:

In my September 2016 report, I expressed my opinion that the manner in which Dr. Bhambhani obtained and prescribed NECC's PF-NPA was substandard. Her testimony of January 9, 2018 confirms that Dr. Bhambhani's choice of compounded MPA was a practice wide decision, not one based upon the specific needs of individual patients. This is further confirmed by the listing of patients who had already undergone treatment at Box Hill for PF-MPA which was used in other patients. Further, five, 5 ml vials were obtained for each of those names, far more than any one patient would be treated with. Her testimony thus confirms, in my opinion, her failure to comply with Maryland law and minimum standards of care of care regarding the safe prescription of medications. Her failure to meet these standards increased the risk of harm to Brenda Rozek.

It is my expert medical opinion, to a reasonable degree of medical probability, that Ms. Brenda Rozek died as a direct result of infection due to the fungus *Exserohilum rostratum*. This fungus was introduced into her body by injection of a contaminated steroid solution manufactured by NECC and administered by Dr. Bhambhani at Box Hill Surgical Center in Abingdon, MD.

- On August 31, 2012 Brenda Rozek received a cervical epidural injection with 80 mg of fungus contaminated MPA from NECC (lot # 0629012).
- Starting on or around September 5, 2102 her ongoing headache changed and she developed progressively worsening headaches and other symptoms that included a sensation of feeling lightheaded, dizzy and nauseous. Her condition continued to deteriorate and she also developed double vision, difficulty standing, light sensitivity, slurred speech, right sided weakness, left facial droop and decreasing levels of alertness. During this process she was admitted to Union Hospital in Elkton, MD.
- Testing of cerebrospinal fluid (CSF) obtained by lumbar puncture on September 10, 2012 showed that she had meningitis (CSF with elevated white blood cells count and

- protein and low glucose level). Imaging of the brain with magnetic resonance imaging (MRI) that day showed abnormalities in the brainstem.
- She was transferred to Johns Hopkins Hospital on September 11, 2012 with symptoms with severely depressed mental status.
 - Her course was further complicated by hydrocephalus for which an intraventricular catheter was inserted on September 13, 2012. Imaging on that day showed increase in pontine and medullary strokes.
 - Despite treatment with multiple different antibiotics, including the antifungal liposomal amphotericin B her condition progressed. She succumbed to the infection and was pronounced dead on September 16, 2012
 - Cultures of CSF obtained on September 14, 2012 and at post mortem examination showed *Exserohilum rostratum*. Autopsy findings showed that this fungal infection had penetrated into blood vessels leading to blood clotting (thromboses) and extensive destruction and bleeding in the spinal cord and multiple parts of the brain. These in turn led to the patient's death.

Conclusions and outlook for the future

This tragic outbreak involved over 750 patients and caused 64 deaths nationwide according to the CDC counts. In Maryland there were 26 cases (almost all with meningitis) and 4 deaths attributable to the outbreak (including Brenda Rozek). The medical community's response to this outbreak required the efforts of thousands of clinicians and public health officials at federal, state, and local levels. Patients suffered significant injuries from the infection and its therapy, and in a number of cases died as a result of their infections. It is not known what the future holds for those patients who appear to have cleared the infection. For example, will infection return in patients who have stopped antifungal therapy? Instances of relapse have been reported, including one patient whose infection recurred 21 months after cessation of therapy, prompting CDC experts to warn clinicians and patients that they "should remain watchful for symptoms of infection in patients exposed to the contaminated PF- MPA, because fungal infections can develop slowly and are difficult to eradicate".

Documents Reviewed for this Report:

1. Maryland Department Health and Mental Hygiene medical files, test reports and spreadsheets on Box Hill Surgery Center patients administered NECC MPA-PF at Box Hill during procedures.
2. Lyons, Jennifer L., *et al*, *Fatal Exserohilum Meningitis and Central Nervous System Vasculitis After Cervical Epidural Methylprednisolone Injection*, *Annals of Internal Medicine* 157:11, p.835 (Dec. 4, 2012) (Brenda Rozek case report).
3. Smith, Rachel M., *et al*, *Fungal Infections from Contaminated Methylprednisolone*, *New England J. of Med.* 369;17, p. 1598 (Oct. 24, 2013).
4. Tom M. Chiller, *Clinical Findings for Infections from Methylprednisolone Caused by Methylprednisolone Injections*, *New England J. of Med.* 369;17, p. 1610 (Oct. 24, 2013).
5. Wilson, Lucy E., *et al.*, *Fungal Meningitis From Injection of Contaminated Steroids: A Compounding Problem*, *J. American Medical Association*, 308:23 p 2481(Dec.19, 2012).
6. Deposition transcript of Dr. Ritu Bhambhani, M.D. (February 10, 2016)
7. Bhambhani Deposition Exhibits Nos. 1062, 1063, 1064 and 1065.

8. Deposition transcript of Nurse Andrew Vickers, R.N.
9. Vickers Deposition Exhibits Nos. 1148, 1149 and 1150.
10. Deposition transcript of Dr. Lucy Wilson, M.D.
11. Copies of Box Hill's NECC Prescription Orders forms used to obtain MPA-PF by mail order and packing slips from NECC.
12. Maryland Statute on prescription requirement (MD. Health Code Section 21-220.
13. Board of Pharmacy Newsletter – Fall, 2012.
14. Kauffman CA, Malani AN. *Fungal Infections Associated with Contaminated Steroid Injections*. Microbiol Spectr. 2016;4(2).
15. Pettit AC, Malani AN. *Outbreak of fungal infections associated with contaminated methylprednisolone acetate: an update*. Curr Infect Dis Rep. 2015;17(1):441.
16. Moudgal V, Singal B, Kauffman CA, Brodkey JA, Malani AN, Olmsted RN, et al. *Spinal and paraspinal fungal infections associated with contaminated methylprednisolone injections*. Open Forum Infect Dis. 2014;1(1):ofu022.
17. Casadevall A, Pirofski LA. *Exserohilum rostratum fungal meningitis associated with methylprednisolone injections*. Future Microbiol. 2013;8(2):135-7.
18. Simitsopoulou M, Walsh TJ, Kyrpitzis D, Petrakis V, Kontoyiannis DP, Perlin DS, and Roilides E. Methylprednisolone impairs conidial phagocytosis but does not attenuate hyphal damage by neutrophils against *Exserohilum rostratum*. *Medical Mycology*, 2015, 53, 189–193.
19. Farmakiotis D, Shirazi F, Zhao Y, Saad PJ, Albert ND, Roilides E, Walsh TJ, Perlin DS, and Kontoyiannis DP. *Methylprednisolone Enhances the Growth of Exserohilum rostratum In Vitro, Attenuates Spontaneous Apoptosis, and Increases Mortality Rates in Immunocompetent Drosophila Flies*. The Journal of Infectious Diseases 2014; 210:1471–5.
20. Deposition transcript of Dr. Ritu Bhambhani, M.D. (January 9, 2018)
21. Deposition transcript of Neil E. Rozek
22. Rozek exhibits 1-5.
23. Bhambhani exhibits 1-8.

My fee for research, writing, consultations and testimony at deposition and trial in the cases at issue is \$500 per hour.

I reserve the right to supplement, modify or amend this letter report after further research and review of additional material, including depositions.

Respectfully submitted on January 22, 2018

A handwritten signature in black ink, appearing to read 'S. Shoham', followed by a horizontal line.

Shmuel Shoham, MD

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